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**Evidence for the outcomes and impact of clinical pharmacy – Context of UK hospital
pharmacy practice**

Raliat Onatade*

1. King's College London, Institute of Pharmaceutical Sciences, London, United Kingdom
2. Middlesex University, Department of Natural Sciences, Faculty of Science and Technology, Middlesex University, The Burroughs, London NW4 4BT

*Author for correspondence

Email: raliat.onatade@kcl.ac.uk

Tel: +44 794 1108583

Postal address: Pharmacy Department, Barts Health NHS Trust, London E1 2ES

Dr. Sandra Appiah

Senior Lecturer in Biosciences, Department of Natural Sciences, Faculty of Science and Technology, Middlesex University, The Burroughs, London NW4 4BT

Prof. Martin Stephens

Visiting Professor, University of Portsmouth, Wessex Pharmacy LPN Chair, Oakley Road, Southampton, SO16 4GX

Prof. Hemda Garelick

Professor of Environmental Science and Public Health Education, Department of Natural Sciences, Faculty of Science and Technology, Middlesex University, The Burroughs, London NW4 4BT

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Abstract

Objectives: The role of clinical pharmacists in hospitals has evolved and continues to expand. In the UK, outside a few national policy drivers, there are no agreed priorities, measures or defined outcomes for hospital clinical pharmacy (CP). This paper aims to 1) highlight the need to identify and prioritise specific clinical pharmacy roles, responsibilities and practices that will bring the greatest benefit to patients and health-systems and 2) describe systemic weaknesses in current research methodologies for evaluating clinical pharmacy services and propose a different approach

Method: Published reviews of CP services are discussed using the economic, clinical and humanistic outcomes (ECHO) framework. Recurring themes regarding study methodologies, measurements and outcomes are used to highlight current weaknesses in studies evaluating CP.

Results: Published studies aiming to demonstrate the economic, clinical or humanistic outcomes of clinical pharmacy often suffer from poor research design and inconsistencies in interventions, measurements and outcomes. This has caused difficulties in drawing meaningful conclusions regarding clinical pharmacy's definitive contribution to patient outcomes.

Conclusion: There is a need for more research work in NHS hospitals, employing a different paradigm to address some of the weaknesses of existing research on clinical pharmacy practice. We propose a mixed-methods approach, including qualitative research designs, and with emphasis on cost-consequence analyses for economic evaluations. This approach will provide more meaningful data to inform policy and demonstrate the contribution of hospital clinical pharmacy activities to patient care and the NHS.

Key Messages

What is already known on this subject

- Clinical Pharmacy is a diverse, complex discipline and clinical pharmacy activities are not easily defined or described
- It is important to robustly show the benefits of clinical pharmacy, in order to justify resource use and to prioritise and measure activities
- Studies purporting to demonstrate the outcomes of clinical pharmacy activities are often criticized due to methodological flaws, poor intervention descriptions and weak conclusions

What this study adds

- The current positivist mindset is weakening the case for clinical pharmacy. There is a need for a new research approach for studying and evaluating clinical pharmacy interventions
- Mixed-methods studies, incorporating quantitative and qualitative methodologies are more appropriate for evaluating the outcomes of clinical pharmacy
- Cost-consequence analyses are more suitable for evaluating the economic outcomes of clinical pharmacy

Introduction

Clinical pharmacy (CP) is a relatively new healthcare discipline, compared to professions such as medicine and nursing. Traditionally, pharmacists were solely concerned with procurement, dispensing, manufacturing and supply of drugs[1]. The official development of CP in the UK began in 1970, with the publication of the government-commissioned 'Noel Hall Report'[2]. Since then, several influential policy documents have been published which have contributed to the development of CP in the UK (see supplementary information). This has led to CP being advocated as vital to the optimal and safe care of patients[3]. Notably, the development of CP in mainland Europe is more variable although expanding [4–6]. Despite the widespread support for CP in hospitals however, there is no agreement within the profession on which components of practice are most important. Moreover, research into the outcomes of CP has not kept pace with the developments in practice.

The UK National Health Service (NHS) is under severe financial pressure, a situation which is likely to remain for the foreseeable future [7]. Medicines remain the most common therapeutic intervention offered to patients and their costs are significant. The NHS spends £6.7 billion on hospital medicines annually[8]. Most NHS trusts spend between 5 and 10% of their total costs on drugs[8] and medicines expenditure increases by an average of 15% every year[9]. Significant resources are invested by trusts to secure their CP workforce. Annually, £0.6 billion is spent on hospital pharmacy services and in 2015/16 pay costs of hospital pharmacists alone averaged nearly £300,000 per 100 beds[10]. It is therefore important that these resources are deployed such that they give greatest benefits.

This paper explores the complexities of hospital clinical pharmacy practice and the consequent difficulties producing robust research evidence on the effectiveness of clinical pharmacy. The aim is to evaluate and highlight the quality of evidence and to suggest an alternative approach for researcher-practitioners.

The evolving role of clinical pharmacists

The complexity of clinical pharmacy practice is reflected in the fact that various definitions have been proposed. In the literature, the terms clinical pharmacy ‘services’, ‘activities’ and ‘interventions’ are used interchangeably[11]. The difficulties in agreeing a single definition of clinical pharmacy relate to the diverse nature of the discipline. This is problematic for researchers and impedes the development of a coherent vision.

Clinical pharmacy is concerned with both medicines policy and the treatment of patients, with the aim of achieving optimal use of medicines[11,12]. Additional aspects of CP, as advocated by The European Society of Clinical Pharmacy (ESCP), the Societe Francaise de Pharmacie Clinique (SFPC) and the United Kingdom Clinical Pharmacy Association (UKCPA) are concerned with attributes of the pharmacist that allow ‘the appropriate, effective and safe use of medicines’[13]. The role of clinical pharmacy has also expanded to include pharmaceutical care – providing drug therapy to achieve “definite outcomes that improve a patient’s quality of life” [14]. Medicines optimisation is a more recent, overarching concept that considers both clinical pharmacy activities and pharmaceutical care[15].

Hospital clinical pharmacists interact with patients on wards, on multi-professional ward rounds or in clinic settings to treat, monitor and advise on the use of medicines. However, clinical pharmacy clearly encompasses more than just direct patient care. Therefore, activities such as production of guidelines and policies, advising on drug expenditure controls, training and education of other healthcare professionals are also included. The relationships between clinical pharmacy, pharmaceutical care and medicines optimisation are represented in Figure 1 and a list of typical CP activities is provided in Box 1.

Figure 1 here

Box 1 here

Figure 1. The relationship between clinical pharmacy, pharmaceutical care, and medicines optimisation

Box 1. Examples of typical hospital clinical pharmacy activities

Medicines reconciliation - Steps taken to verify that a patient's list of medication is not unintentionally changed when the patient moves from one care setting to another
Prescription monitoring/Prescription review - Checking patients' prescriptions for appropriateness or mistakes and then making recommendations to doctors
Prescribing advice - Helping prescribers to choose the right medicines, doses, administration method etc. for individual patients
Dose adjustments - Changing the dose of a drug to make it more appropriate for the patient
Pharmacokinetic and therapeutic drug level consultations - For drugs which have a narrow gap between therapeutic and toxic doses, advising on blood level sampling and interpreting the results
Medication administration advice - Advising nursing staff on the best way to administer a medicine, or choosing the correct form of the medicine to administer against a prescription
Disease or drug-specific outpatient clinic services - E.g. participating in or leading respiratory, diabetes, hypertension or high-risk drug clinics to optimise treatment and prevent adverse effects
Patient education and patient consultations - Advising and educating individuals or groups of patients to help them understand their medicines and adhere to the treatment plan that they have agreed to

Medication error reporting and resolution - Reporting medication errors to support organizational learning from mistakes and to prevent errors from being repeated
Adverse drug reaction reporting - Reporting avoidable or unavoidable reactions to drugs
Antimicrobial stewardship - Implementing and monitoring policies and systems for promoting and monitoring appropriate use of antimicrobial drugs
Medication safety leadership and initiatives
Training and education of other healthcare staff
Managing formularies and the entry of new drugs
Guideline and protocol writing
Clinical audit
Advising on or managing the medicines budget
Ensuring the appropriate, safe and secure handling of medicines within the hospital (sometimes called medicines management)

Source: Stephens M. Hospital Pharmacy, 2011[16]

This table demonstrates the span and complexity of clinical pharmacy services. The list is not exhaustive, however represents more than 50% of typical workload. Clinical pharmacy services are not only delivered by pharmacists. An overview of changing roles in the pharmacy workforce describes how pharmacy technicians have increasingly important clinical responsibilities for patient care, including medication history taking, prescription checking and supporting patient adherence[17].

Levels of clinical pharmacy service provision are not consistent between hospitals. The most recent policy report concerning hospital CP in the UK was published in January 2016[9]. This report decries the significant variation in the scope of CP activities between hospitals but also recommends that hospitals deploy 80% of their pharmacist resource towards direct patient care and medicines optimisation. In these financially constrained times, this will only be a good use of resource if one knows where benefits are most likely to be seen, and how to measure them. It is therefore essential that services are prioritised, and that this prioritisation is underpinned by appropriate evidence.

Current evidence on the outcomes and benefits of clinical pharmacy

There are few agreed priorities and measures for hospital clinical pharmacy or its core 'patient-facing' medicines optimisation activities. Common policy- or finance-driven activities are few, and include medicines reconciliation, antimicrobial stewardship, medication safety and general 'medicines management'. The Royal Pharmaceutical Society (RPS) published the first Professional Standards for Hospital Pharmacy Services for Great Britain in 2012 (refreshed in 2014)[18]. There are ten overarching standards, and they provide hospital pharmacy departments with structure and guidance regarding expected services and responsibilities. Similar to the RPS standards, in 2014 the European Association of Hospital Pharmacists (EAHP) developed 44 European Statements for Hospital Pharmacy services. The statements articulate objectives for the delivery of hospital pharmacy services in European health systems [19]. However, the nature of both the RPS Standards and the EAHP Statements is such that they offer little help with prioritising services to be developed (or indeed services to disinvest from); they are also not measurable indicators. Extracts from the standards and statements documented can be seen in Box 2.

Box 2. Extracts from the Royal Pharmaceutical Society Professional Standards for Hospital Pharmacy Standards[18] and European Association of Hospital Pharmacy Statements for Hospital Pharmacy Services [19]

RPS Standard 2 Episode of Care

Patients' medicines requirements are regularly assessed and responded to, in order to keep them safe and optimise their outcomes from medicines.

2.1 On admission or at first contact

Patients' medicines are reviewed to ensure an accurate medication history, for clinical appropriateness and to identify patients in need of further pharmacy support.

a. The pharmacy team provides the leadership, systems support and expertise that enables a multidisciplinary team to:

- Reconcile patients' medicines as soon as possible, ideally within 24 hours of hospital admission to avoid unintentional changes to medication
- Effectively document patients' medication histories as part of the admission process
- Give patients access to the medicines that they need from the time that their next dose is needed
- Identify patients in need of pharmacy support and pharmaceutical care planning
- Identify potential medicines problems affecting discharge (or transfer to another care setting) so that they can be accommodated to avoid extending patients' stays in hospital.

2.2 Care as an inpatient

Patients have their medicines reviewed by a clinical pharmacist to ensure that their medicines are clinically appropriate, and to optimise their outcomes from their medicines.

- a. Pharmacists regularly clinically review patients and their prescriptions to optimise outcomes from medicines (timing and level of reviews adjusted according to patient need and should include newly prescribed medicines out of hours) and take steps to minimise omitted and delayed medicine doses in hospitals.
- b. Patients targeted for clinical pharmacy support have their medicines' needs assessed and documented in a care plan that forms part of the patient record.
- c. Pharmacists attend relevant multidisciplinary ward rounds, case reviews and/or clinics.
- d. Patients, medical and nursing teams have access to pharmacy expertise when needed.
- e. The pharmacy team provides the leadership, systems support and expertise that enables patients to:
 - Bring their own medicines into hospital with them and self-administer one or more of these wherever possible
 - Have their own medicines returned at discharge where appropriate.

EAHP Statements Section 4: Clinical Pharmacy Standards

4.1 Hospital pharmacists should be involved in all patient care settings to prospectively influence collaborative, multidisciplinary therapeutic decision-making; they should play a full part in decision making including advising, implementing and monitoring medication changes in full partnership with patients, carers and other health care professionals.

4.2 All prescriptions should be reviewed and validated as soon as possible by a hospital pharmacist. Whenever the clinical situation allows, this review should take place prior to the supply and administration of medicines.

4.3 Hospital pharmacists should have access to the patients' health record. Their clinical interventions should be documented in the patients' health record and analysed to inform quality improvement interventions.

4.4 All the medicines used by patients should be entered on the patient's medical record and reconciled by the hospital pharmacist on admission. Hospital pharmacists should assess the appropriateness of all patients' medicines, including herbal and dietary supplements.

4.5 Hospital pharmacists should promote seamless care by contributing to transfer of information about medicines whenever patients move between and within healthcare settings.

4.6 Hospital pharmacists, as an integral part of all patient care teams, should ensure that patients and carers are offered information about their clinical management options, and especially about the use of their medicines, in terms they can understand.

4.7 Hospital pharmacists should inform, educate and advise patients, carers and other health care professionals when medicines are used outside of their marketing authorisation.

4.8 Clinical pharmacy services should continuously evolve to optimise patients' outcomes.

Researchers have highlighted the paucity of robust research regarding the impact of CP services on organisational and patient outcomes, as well as the lack of information to support the most efficient use of available resources [20–23]. A review of the impact of clinical pharmacy services on health-related quality of life found that methodologies had improved, but studies often did not include a control group[20]. Perez et al.[21] advocate improvements in the design of CP economic evaluation studies. The authors explain how relatively minor changes would improve study rigour. Broad and unclear monitoring targets lead to inconclusive evidence in the evaluation of the impact of CP services. More conclusive evidence for the effectiveness of clinical pharmacy services are reported when the interventions are rigorously defined, in specific medical conditions, and when there are unequivocal outcomes[24]. Often, pharmacists are sole practitioners when providing specialist services which makes unpicking and measuring their individual clinical contributions relatively straightforward. However, most hospital clinical pharmacists work in multidisciplinary teams where linking patient outcomes and pharmacy input is difficult to achieve. This lack of outcome measurement leads to lack of evidence, thus perpetuating the status quo. Clearly, identifying

criteria for measuring clinical pharmacy services should be an important aim. Some researchers have attempted to develop performance indicators[25,26]. An issue still to be overcome is that the indicators for hospital clinical pharmacy found in the literature are all process-based; they measure inputs, rather than outcomes. Fernandes and colleagues[27] published a Canadian consensus list of eight Key Clinical Pharmacy Key Performance Indicators (cpKPIs) with evidence supporting an impact on patient outcomes with a direct link to patient care. This work represents the most systematic approach so far towards the development of Key Performance Indicators. The available evidence on the outcomes and impact of hospital clinical pharmacy services therefore still merits exploration.

The ECHO model

The framework for assessing Economic, Clinical and Humanistic Outcomes (ECHO)[28] is a useful tool for framing the impacts of CP. Using the ECHO model (as described below and in Table 1), we illustrate the challenges with measuring outcomes of CP. The approach used is a narrative overview of reviews of CP services published in the international literature. To provide a complementary context, where there is a relatable EAHP Statement[17], we include this in the discussion.

Table 1. Summaries and critical evaluations of studies of Economic, Clinical and Humanistic Outcomes (ECHO) of clinical pharmacy services

Outcomes evaluated	Title and year of article	No. of studies (set in UK hospitals)	Summary of findings	Reported limitations of included studies
Economic	<i>Economic effects of clinical pharmacy interventions: a literature review</i> [29] (2008)	21 (0)	Cost–benefit analyses suggested that general clinical pharmacy interventions are associated with cost savings.	Absence of control groups, limited scope of costs and outcomes, exclusion of costs of providing the service and absence of incremental cost analyses or benefit: cost ratios.
	<i>Economic Evaluations of Clinical Pharmacy Services: 2006–2010</i> [30] (2014)	25 (1)	CP services were generally considered cost-effective or provided a good benefit-cost ratio.	Variability in clinical outcomes contributed to variations in the cost-effectiveness findings. Future studies should focus on identifying specific aspects of CP services that contribute to improved clinical outcomes and efficiency.
	<i>Economic evaluations of clinical pharmacist interventions on hospital inpatients: a systematic review of recent literature</i> [31] (2014)	22 (0)	Overall, pharmacist interventions had a positive impact on hospital budgets and continue to provide cost-savings.	Impossible to determine which interventions were most beneficial because interventions and outcome measures were so disparate.
Economic & Clinical	<i>The economics of medicines optimization: policy developments, remaining challenges and research priorities</i> [32] (2014)	107 (0)	There was a large evidence base on the effectiveness of interventions to improve the suboptimal use of medicines; the cost-effectiveness evidence is much smaller.	The available evidence is insufficient to assess the effectiveness and cost-effectiveness of medicines optimisation interventions.

Outcomes evaluated	Title and year of article	No. of studies (set in UK hospitals)	Summary of findings	Reported limitations of included studies
Economic and Humanistic	<i>Humanistic and economic outcomes of pharmacist-provided medication review in the community-dwelling elderly: A systematic review and meta-analysis</i> [33] (2016)	25 (0)	The findings suggest that the humanistic and economic outcomes of pharmacist-provided medication review are similar to those of usual care.	All studies had a high to medium risk of bias. Components of generic HRQoL measures may not be significantly influenced by medication review. There was a failure to differentiate between necessary spending and undesirable spending. In many studies, follow-up may not have been long enough to detect changes in outcomes
Economic, Clinical & Humanistic	<i>Economic effects of pharmacists on health outcomes in the United States: A systematic review</i> [34] (2010)	126 (0)	Twenty studies showed results favouring pharmacist-provided care. Reduced length of stay and drug costs were seen for inpatients when pharmacists managed specific drug therapies; varied results for humanistic outcomes.	Partial cost analyses, focus on drug costs and not cost of service, poor design and other flaws limited the majority of studies.
	<i>Medication reviews by clinical pharmacists at hospitals lead to improved patient outcomes: a systematic review</i> [35](2013)	31 (1)	A positive effect on medication use and costs, quality of prescribing, satisfaction with the service and both positive and insignificant effects on health service use were seen in some studies.	The majority of the included studies used weak methodologies.
	<i>The role of the pharmacist in optimizing pharmacotherapy in older people</i> [36] (2012)	16 RCTs (2 RCTs), 9 systematic reviews	Proactive action of pharmacists improved pharmacotherapy for older patients. Mixed evidence on the impact of pharmacists' interventions on health outcomes, quality of life or cost effectiveness of care.	Single-centre studies, limited generalisability, contamination bias. Economic analyses are needed.

Outcomes evaluated	Title and year of article	No. of studies (set in UK hospitals)	Summary of findings	Reported limitations of included studies
Clinical & Humanistic	<i>Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis</i> [37] (2008)	32 (3)	Possible weak effects on knowledge, adherence and reductions in number of drugs prescribed. Insufficient data to know whether quality of life is improved. No effect on reducing mortality or hospital admission.	Heterogeneity of studies. Inconsistent reporting of outcomes. Some of the studies may have been susceptible to bias.
Clinical	<i>Clinical Pharmacists and Inpatient Medical Care: A Systematic Review</i> [38] (2006)	36 (0)	The addition of clinical pharmacist services in the care of inpatients generally resulted in improved care, with no evidence of harm.	Small sample sizes, single institution and limited generalisability.
	<i>Medication review in hospitalised patients to reduce morbidity and mortality</i> [39] (2013)	5 (0)	No effect on mortality or readmissions. There was a reduction in ED contacts. Medication review should not be undertaken outside the context of robust trials with long follow-up.	In three of the studies, either a physician or clinical pharmacologist was also involved in the actual reviews, and any unique contribution of the clinical pharmacist could not be assessed.
	<i>The effect of early in-hospital medication review on health outcomes: a systematic reviews</i> [40] (2015)	7 (0)	No effect on length of hospital stay, mortality or readmissions. A pooled effect on ED revisits failed to reach statistical significance.	Methodologically flawed, with a high risk of selection bias. Wide variations in the interventions studied and missing data.
	<i>Pharmacist-led interventions to reduce unplanned admissions for older people: a systematic review and meta-analysis of randomised controlled trials</i> [41] (2014)	20 (3)	Unplanned admissions not affected by hospital or community pharmacist interventions. An effect was found with older people with heart failure, but further confirmation is needed due to heterogeneity.	Moderate to high risk of bias.

Outcomes evaluated	Title and year of article	No. of studies (set in UK hospitals)	Summary of findings	Reported limitations of included studies
Humanistic	<i>An update on evidence of clinical pharmacy services' impact on health-related quality of life</i> [20] (2006)	36 (2)	Limited evidence of the impact of a few CP interventions on short-term HRQoL.	Compared with studies published prior to 1999, studies had improved: longer length of follow-up, a wider breadth of clinical services were evaluated and several studies were well designed and methodologically rigorous.

RCT = Randomised Controlled Trial, CP = Clinical Pharmacy, ED = Emergency Department, HRQoL = Health-Related Quality of Life

Economic outcomes: EAHP Statement 2.3 refers to the economic outcomes of CP, with reference to the requirement for hospital pharmacists to co-ordinate medicines formularies, linked to evidence on patient outcomes and pharmacoeconomic evaluations. The American College of Clinical Pharmacy has commissioned reviews of economic evaluations of CP services since 1988. In the latest article in this series, published in 2014[30], the authors found that benefit to cost (B:C) or Incremental Cost-Effectiveness Ratios (ICERs) were reported or could be calculated for just eight studies. The authors also reported that the quality of studies and the pharmacoeconomic evaluations had improved since their previous review, published in 2008. However, significant methodological weaknesses were still identified. In the most recent systematic review of economic evaluations of inpatient clinical pharmacist interventions, Gallagher and colleagues[31] found no studies from the UK. Interventions examined included antimicrobial management, medicines optimisation, specialist input into areas such as neurosurgery and intensive care, and multi-dimensional services. All of these are hospital CP services currently provided in the UK. Three studies were assessed as 'good' quality, while seven were judged to be of poor quality. Only one paper[42] included all criteria for an appropriate economic evaluation according to the Consolidated Health Economic Evaluation Reporting Standards[43] criteria. Interestingly, this study[42] found that the in-hospital clinical pharmacist service was probably not cost-effective. Elliot et al.[44] provide a comprehensive critique of the methodological quality of 31 cost-effectiveness studies of pharmacist interventions. Twelve of the studies were from the UK, with just two based in hospitals. Overall, they found a range of factors contributing to the general lack of consensus about the effectiveness of pharmacy services. The main ones were poor study design and data analysis, as well as variations in intervention design and delivery, resource use, measurement and outcomes[44].

Clinical outcomes: Many of the objectives included in EAHP Statement 4 – Clinical Pharmacy Services - are applicable to ensuring appropriate clinical outcomes of CP. Specifically, statements 4.1, 4.2, 4.4, 4.6 and 4.8 refer to influencing therapeutic decisions, prescription and

medication review, medicines reconciliation, provision of appropriate information and optimising outcomes. Kaboli et al. [38] found that clinical pharmacists practising in the inpatient setting improved the quality, safety and efficiency of care. They also suggested that more research is needed to better understand the role of clinical pharmacists and the clinical areas most likely to benefit. They pointed out the limitations of the reviewed studies (small sample sizes, single institution and limited generalisability). Medication review is an area of practice that is common, to a greater or lesser degree, to all UK hospital CP services. It is described in the literature as a systematic and structured assessment of the drug treatment of an individual patient, with the aims of optimising the quality, safety and appropriate use of their medicines and reducing medication-related problems, either by a recommendation or by a direct change. It may or may not include a discussion with the patient[37,45]. Holland et al. [37] in their systematic review and meta-analysis of randomised controlled trials (RCTs) to assess the effects of medication reviews for older people, only found possible weak effects on patients' knowledge and adherence and reductions in number of drugs prescribed. A Cochrane Review of medication reviews[39] found a reduction in emergency department contacts but no effect on mortality or readmissions. The authors concluded that medication review should not be undertaken outside the context of high quality trials with long follow up. Graabaek and Kjeldsen conducted a systematic mini-review of 31 hospital-based studies[35]. They describe positive effects of medication reviews on medication use and satisfaction with the service, but also comment on the weak methodologies of the included studies. Many of the aims of medicines optimisation mirror those of medication reviews. Faria et al.[32] reviewed the evidence on the effectiveness of medicines optimisation. They concluded that more research on outcomes and which pharmacist duties are most beneficial to patients is needed. Hohl et al.[40] looked at early in-hospital medication reviews by pharmacists. Given the weaknesses in the reviewed studies, the authors recommended high quality randomised trials to fill the gaps in the evidence. However, RCTs may also not provide the required robust evidence. Many of the studies discussed above included RCTs with significant weaknesses. A review of RCTs of pharmacist-led interventions to reduce unplanned admissions or readmissions also found a lack of effect of interventions[41].

Humanistic outcomes: Literature on humanistic outcomes is much sparser than the other two dimensions. The main humanistic outcomes that studies evaluate are patient satisfaction and health-related quality of life (HRQoL). The EAHP Statements do not mention hospital pharmacists' responsibility for humanistic outcomes, although one statement (4.6) does refer to providing information to patients on the use of their medicines in terms they can understand. Pharmacy researchers have found limited or mixed evidence of the impact of pharmacists' interventions on quality of life. Pickard et al.[20] in a 2006 overview of 36 studies (two from the UK), found limited evidence of the impact of a few CP interventions on short-term HRQoL. In their systematic review and meta-analysis, Holland and colleagues[37] could not find sufficient evidence to show that medication reviews for older people improved quality of life. Chisholm-Burns et al.[34] also found that results for humanistic outcomes varied. Spinewine et al.[36] reviewed the literature on the role of pharmacists in optimising pharmacotherapy in older people. They also concluded that there is mixed evidence of the impact of pharmacists' interventions on quality of life. There have therefore been calls for more sensitive outcome measures for pharmaceutical care services, including a medicines related quality of life tool[22].

Summary and suggestions for future work

In order to demonstrate the benefit of CP, as for all healthcare interventions, evidence of its effectiveness in improving patient care and optimising resources is needed to justify and prioritise services. Currently, the quality of evidence supporting broad-based CP services is limited and outcomes have not been consistently demonstrated. There is little clarity on which specific CP roles, responsibilities and practices bring greatest benefit to patients, organisations or health service priorities, so it is unclear which should be prioritised or made universally available. Table 2 summarises those beneficial outcomes supported by systematic reviews.

Table 2. Benefits of clinical pharmacy interventions and services as indicated by the literature

Outcome	Benefits described in the literature
Economic/Financial	Savings on drug costs Cost-avoidance
Clinical	Improved quality of prescribing Reduced numbers of medications Resolution of drug-related problems Therapeutic goal attainment in specific conditions
Humanistic	Patient knowledge of their medicines Adherence

See supplementary file 2 for a reading list of studies describing benefits of specific clinical pharmacy interventions.

Research into the outcomes of UK hospital clinical pharmacy practice is scarce in the literature. This is possibly because CP is well-embedded in the UK National Health Service and therefore there is little motivation to demonstrate the benefits. However, the level of provision is not consistent across the health service because of a lack of evidence, aggravated by sub-optimal research. Research is emerging from mainland Europe, where CP is currently less well established. It remains to be seen if published outcomes from Europe carry enough weight to influence policy on the development of CP.

Economic evaluations of CP interventions need to be more methodologically robust and follow health economic guidelines more closely. However, the standard cost-benefit, cost-utility and cost-effectiveness analyses may not always be the most appropriate studies to conduct. These require benefits to be aggregated into a single outcome (for example, a monetary figure or a health-related quality of life measure), without allowing for the possibility that the impact of CP interventions may extend beyond this type of quantification. Cost-consequence analyses

(CCAs) do not try to put all the costs and benefits into the same units. CCAs allow for different types of benefits that cannot be combined. By disaggregating the consequences (outcomes), different weights can be applied to the various benefits, depending on one's priorities[46]. The National Institute for Health and Care Excellence is now explicit about conducting cost-consequence analyses (CCAs) of public health interventions, in recognition of the fact that CCAs can take into account the wider benefits of an intervention[47]. Given the complexity and multiple aims of CP services, CCAs offer many advantages over other economic evaluations[48]. Perhaps it is time that CCAs cease to be seen as a 'lesser' form of economic evaluation when it comes to CP interventions.

As described above, CP practice research is often considered to have been poorly conducted (according to the accepted norms). The emphasis in the profession on mainly reporting and assessing evidence from quantitative studies is problematic and may in fact be weakening the case for CP. It is likely that studies have not measured those outcomes that CP interventions can influence.[21] RCTs and similar types of quantitative evidence reflect the positivist-realist epistemology which dominates clinical medicine[49,50]. Slade and Priebe[51], discussing the role of RCTs in mental health interventions, argue that the medical establishment's insistence on dismissing all other types of evidence ignores the contributions from other methodologies in answering research questions. The same point could be made that CP interventions can often not be standardised or strictly defined. Some pharmacy researchers have urged the inclusion of a social science slant into pharmacy practice research[52]. In particular, the value of knowledge which arises from social sciences research, reflection, actions and practice experience[53] is rarely considered in the scholarly literature on CP practice. Investigations into humanistic and clinical outcomes specifically, require different methodologies to understand the benefits that are valued by patients and other parties and to uncover any 'pharmacy-sensitive' effects. For example, as there are various factors that affect the rate of hospital admission, it is unlikely to be a sensitive outcome measure for CP[41]. More

humanistic outcomes urgently need to be demonstrated; qualitative methods are required to generate theories on what these might be.

It is our view that a shared understanding of the aims and outcomes of CP is needed. The approach to achieving this should be inclusive and will integrate both institutional and patient-centred goals. Research into the outcomes of CP interventions will continue to be criticised for its lack of rigour until practitioners embrace alternative strategies. As well as cost-consequence analyses, CP researchers should consider conducting robust qualitative and mixed-method (qualitative and quantitative) studies, utilising methodologies from evaluation, improvement and implementation science disciplines.

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Supplementary FILE 1 . Policy documents charting the history of the development of Hospital Clinical Pharmacy

Author and Year	Document Title	Summary
Noel Hall, 1970	Report of the Working Party on the Hospital Pharmaceutical Service	Recommended pharmacists' professional and scientific skills be used to ensure the safe, efficient and economical use of drugs. Within a few years, hospital pharmacy services started to become 'patient-centred' rather than 'product-focused'.
Clucas, K. Nuffield Foundation, 1986	The Report of a Committee of Inquiry appointed by the Nuffield Foundation	Defined CP as <i>"a developing role... in which pharmaceutical skills are systematically applied to medicine usage both at the policy-making level and in the treatment of the individual patient"</i> .
Department of Health, 1988	Health Services Management: the way forward for hospital pharmaceutical services, HC (88) 54	Identified core elements of clinical pharmacy and endorsed hospital clinical pharmacy practice. Clinical Pharmacy becomes government policy.
Crown, J. 1999	Review of prescribing, supply and administration of medicines. Final report	Recommends the development of new categories of prescribers - 'independent' and 'dependent' (later 'supplementary') from among non-doctor healthcare professionals. As a direct result, since 2006, pharmacists have been able to qualify as independent prescribers, theoretically gaining much the same autonomous prescribing rights as doctors.
Department of Health, 2000	Pharmacy in the Future – Implementing the NHS Plan	Clinical pharmacy services should do more ensure best use of medicines in hospitals. Hospital pharmacists should have their time freed up to focus on clinical care. Highlights one-stop dispensing, self-administration of medicines, prescribing in specialist areas, and prescribing take-home medicines as possible ways to make better use of pharmacists' clinical skills.
The Audit Commission, 2001	A Spoonful of Sugar: Medicines Management in NHS Hospitals. Hospitals	Defines medicines management in hospitals – <i>"(it) encompasses the entire way that medicines are selected, procured, delivered, prescribed, administered and reviewed to optimise the contribution that medicines make to producing informed and desired outcomes of patient care"</i> . Makes the case for the role of clinical pharmacy in improving care and reducing costs.
Department of Health, 2003	A Vision for Pharmacy in the New NHS	Highlights the increasing integration of hospital pharmacists into clinical teams and the development of specialised clinical roles.
Department of Health, 2003	Medicines management in NHS Trusts: hospital medicines management framework	Defines standards for the clinical and cost-effectiveness responsibilities of hospital pharmacy services.
Commission for Healthcare Audit and Inspection, 2007	The best medicine: the management of medicines in acute and specialist trusts	Highlights the role clinical pharmacists play in ensuring patient safety. <i>"The involvement of clinical pharmacy staff is clearly a service that benefits the safety of patients..."</i> Uses the amount of clinical pharmacy time available as an indicator of effective medicines management.
Royal Pharmaceutical Society, 2013	Medicines Optimisation: Helping patients to make the most of medicines	Consolidates the term 'Medicines Optimisation' and sets out the role of pharmacists and other health and social care professionals in ensuring individual patients get the best from their medicines.
European Association of Hospital Pharmacy, 2014	European Statements of Hospital Pharmacy	Forty-four statements expressing commonly agreed objectives which every European health system should aim for in the delivery of hospital pharmacy services.
Lord Carter of Coles, 2016	Operational productivity and performance in English NHS acute hospitals: Unwarranted variations	Recommends hospitals ensure 80% of pharmacist resource is spent on clinical / medicines optimisation services – <i>"to deliver optimal use of medicines, make informed medicines choices, secure better value and drive better patient outcomes and 7-day health and care services"</i> .

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